

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) An immunogenic composition comprising an IL-13 element that ~~is capable of driving~~ drives an immune response that ~~recognises~~ recognizes human IL-13 and ~~one or more~~ at least one foreign T-cell epitope~~epitope~~.
2. (Currently amended) An immunogenic composition as claimed in claim 1, wherein the T-cell epitope~~epitope~~ [[are]]~~is~~ foreign with respect to [[both]]human self-proteins and ~~with respect to~~ IL-13 sequence~~sequence~~ from other species.
3. (Currently amended) An immunogenic composition as claimed in claim 1-~~or~~ claim 2, wherein the T-cell helper epitope~~epitope~~ [[are]]~~is~~ a short peptide sequence~~sequence~~ added to the IL-13 sequence-~~or~~ are comprised with a carrier protein.
4. (Currently amended) An immunogenic composition as claimed in claim 3 wherein the carrier protein is selected from the group of: *Haemophilus influenzae* Protein D and CPC (clyta-P2-clyta).
5. (Cancelled)
6. (Currently amended) An immunogenic composition as claimed in claim 3, wherein at least one short T-cell epitope~~epitope~~ [[are]]~~is~~ added to the IL-13 sequence by an event selected from the group of: an addition[[or]]and a substitution~~event within, or at the terminal ends, of the IL-13 sequence by synthetic, recombinant or molecular biological means.~~
7. (Original) An immunogenic composition as claimed in claim 6 wherein the short T-cell epitope is a promiscuous epitope.
8. (Currently amended) An immunogenic composition as claimed in claim 7 wherein the promiscuous epitope is selected from the group of: P2 and P30 from tetanus toxoid.

9. (Currently amended) An immunogenic composition as claimed in claim 1, wherein the IL-13 element comprises the entire human IL-13 sequence, or functional equivalent fragments thereof.
10. (Original) An immunogenic composition as claimed in claim 9 wherein the IL-13 element is in mutated form.
11. (Original) An immunogenic composition as claimed in claim 10, wherein the mutated IL-13 is in the form of a chimaeric IL-13 formed by substituting amino acids with amino acids that are found in equivalent positions within an IL-13 sequence from another mammalian species.
12. (Original) An immunogenic composition as claimed in claim 11, wherein the substitutions occur in areas that are associated with alpha helical regions.
13. (Currently amended) An immunogenic composition as claimed in claim 11[[or 12]] wherein the substitutions involve amino acids taken from more than one different non-human mammalian species.
14. (Currently amended) An immunogenic composition as claimed in claim 1 wherein the IL-13 element [[are]]is human chimaeric IL-13 sequenceessequence which havehaving a similar conformational shape to native human IL-13 whilst havingand sufficient amino acid sequence diversity to enhance its immunogenicity when administered to a human, characterized in that the chimaeric IL-13 immunogen wherein the human chimaeric IL-13 sequence has the sequence of human IL-13 comprising:
 - (a) substitution mutations in at least two of the following alpha helical regions selected from the group of: PSTALRELIEELVNIT, MYCAALESLI, KTQRMLSGF [[or]] and AQFKVKDLLHLKKLFRE[[,]];
 - (b) comprises in unmutated form at least six of the following regions of high inter-species conservation selected from the group of: 3PVP, 12ELIEEL, 19NITQ, 28LCN, 32SMVWS, 50SL, 60AI, 64TQ, 87DTKIEVA, 99LL, and 106LF[[,]]; and
 - (c) optionally comprises a mutation in any of the remaining amino acids, wherein any substitution performed in steps a, b or c is a structurally conservative substitution.

15. (Original) An immunogenic composition as claimed in claim 14, wherein greater than 50% of these substitutions or mutations comprise amino acids taken from equivalent positions within the IL-13 sequence of a non human.

16. (Currently amended) An immunogenic composition as ~~claimed~~ in claim 14[[or 15]], wherein greater than 50% of these substitutions or mutations occur in regions of human IL-13 which are predicted to be alpha helical in configuration.

17. (Currently amended) An immunogenic composition as claimed in claim 14,~~15 or 16~~, wherein the immunogen comprises human chimaeric IL-13 sequence has the sequence of human IL-13 comprising between 2 and 20 substitutions.

18. (Currently amended) An immunogenic composition as claimed in claim 1 wherein the IL-13 element is based on [[an]]a non-human IL-13 sequence wherein the non-human surface exposed regions are substituted for the equivalent human sequences.

19. (Currently amended) An immunogenic composition as claimed in claim 14, wherein the amino acid sequence of human IL-13 comprises conservative substitutions, ~~or substitutions characteristic of amino acids present at equivalent positions within the IL-13 sequence of a non human species, present in at least six of the following[[13]] positions selected from the group of:~~ 8T, 11R, 18V, 49E, 62K, 66M, 69G, 84H, 97K, 101L, 105K, 109E, and 111R.

20. (Currently amended) An immunogenic composition as claimed in claim 19 comprising at least [[6]]six of the following substitutions selected from the group of: 8T to S, 11R to K, 18V to A, 49E to D, 62K to R, 66M to I, 69G to A, 84H to R, 97K to T, 101L to V, 105K to R, 109E to Q, and 111R to T.

Position	Substitution
8	T>S
11	R>K
18	V>A
49	E>D
62	K>R
66	M>I
69	G>A

84	H>R
97	K>T
101	L>V
105	K>R
109	E>Q
111	R>T

21. (Currently amended) An immunogenic composition as claimed in claim 1, wherein the IL-13 element is selected from the following group of: Immunogen 1, Immunogen 11, Immunogen 12 and Immunogen 13.

22. (Currently amended) An immunogenic composition as claimed in claim 1, selected from the following group of: Immunogen 2, Immunogen 3, Immunogen 7, Immunogen 8, Immunogen 9 and Immunogen 10.

23. (Currently amended) An immunogenic composition as claimed in any one of claims 1 to 22claim 1 further comprising a mutation in the human IL-13 element that abolishes the human IL-13 biological activity of the immunogen and is selected from the following group of: E12 to I, S, or Y; E12 to K; R65 to D; S68 to D; and R108 to D.

24. (Currently amended) A method of designing an immunogenic composition as claimed in claim 1 comprising:

(a) taking the sequence of human IL-13 and identifying regions in human IL-13 (SEQ ID NO. 1) that are predicted to form an alpha helical structure[[],]; and

(b) mutating the sequence of human IL-13 within these alpha helical regions to substitute amino acids from the human sequence with amino acids that are either a conservative substitution or are found in equivalent positions within the IL-13 sequence of a different species[[],]; and

(c) attaching or inserting a source of T-cell epitopes that are foreign with respect to any human self epitope and also foreign with respect to any mammalian IL-13 sequence.

25. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen which has a similar conformational shape to native human IL-13 whilst having and sufficient amino acid sequence diversity to enhance its immunogenicity when administered to a human, the method comprising the following steps:

- (a) ~~taking the sequence of human IL-13 and~~ performing at least one substitution mutation in human IL-13 (SEQ ID NO. 1) in at least two of the following alpha helical regions selected from the group of: PSTALRELIEELVNIT, MYCAALESLI, KTQRMLSGF [[or]]and AQFVKDLLLHLKKLFRE[[.]];
(b) preserving at least six ~~of the following~~ regions of high inter-species conservation selected from the group of: 3PVP, 12ELIEEL, 19NITQ, 28LCN, 32SMVWS, 50SL, 60AI, 64TQ, 87DTKIEVA, 99LL, and 106LF[[.]];
(c) optionally mutating any of the remaining amino acids[[.]]; and
(d) attaching a source of T-cell epitopes that are foreign with respect to any human self epitope and also foreign with respect to any mammalian IL-13 sequence, ~~characterised in that wherein~~ any substitution performed in steps a, b or c is a structurally conservative substitution.

26. (Original) A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in claim 25, wherein all four alpha helical regions comprise at least one substitution mutation.

27. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in claim 25, wherein ~~all 11 of the regions are unmutated. there are no mutations at any region of high inter-species conservation.~~

28. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen which has a similar conformational shape to native human IL-13 ~~whilst having and~~ sufficient amino acid sequence diversity to enhance its immunogenicity when administered to a human, the method comprising the following steps:
(a) aligning IL-13 amino acid sequences from different species[[.]];
(b) identifying regions of high variability and high conservation[[.]];
(c) ~~taking the sequence of human IL-13 and mutating human IL-13 (SEQ ID NO. 1)[[it]] in~~ the areas of high variability to substitute amino acids from the human sequence with amino acids that are either a conservative substitution or are found in equivalent positions within the IL-13 sequence of a different species[[.]]; and
(d) attaching a source of T-cell epitopes that are foreign with respect to any human self epitope and also foreign with respect to any mammalian IL-13 sequence[[.]].

29. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in ~~any one of claims~~claim 24 to 28, wherein all greater than 50% of

these substitutions or mutations comprise amino acids taken from equivalent positions within the IL-13 sequence of a non-human species.

30. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in ~~any one of claims~~claim 24 to 28, wherein greater than 50% of these substitutions or mutations occur in regions of human IL-13 which are predicted to be alpha helical in configuration.

31. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in ~~any one of claims~~claim 24 to 28, wherein substitutions or mutations comprise amino acids taken from equivalent positions within at least two non-human IL-13 sequences.

32. (Currently amended) A method for the manufacture of a human chimaeric IL-13 immunogen as claimed in ~~any one of claims~~claim 24 to 28, wherein the immunogen comprises between 6 and 20 substitutions, and most preferably between 6 and 10 substitutions.

33. (Currently amended) An immunogen ~~that is derivable~~derived from ~~any of the methods~~method claimed in ~~claims~~claim 24 to 28, wherein the immunogens are immunogenic, when formulated in an appropriate manner for a vaccine, in a human vaccinee.

34. (Currently amended) A vaccine comprising the ~~immunogen IL13 element~~ as claimed in ~~any one of claims~~claim 1 to 23 or claim 33.

35. (Currently amended) A polynucleotide vaccine comprising a polynucleotide that encodes an ~~immunogen~~IL13 element as claimed in ~~claimed in any one of claims~~claim 1 to 23 or claim 33.

36. (Currently amended) A method of treating an individual suffering from or being susceptible to CPD, asthma or atopic dermatitis, comprising administering to ~~that said~~ individual a vaccine as claimed in claim 34, and thereby raising in that individual a serum ~~neutralising~~neutralizing anti-IL-13 immune response and thereby ameliorating or abrogating the symptoms of COPD, asthma or atopic dermatitis.

Claims 37-38 (Cancelled)

39. (New) An immunogenic composition as claimed in claim 1, wherein the T-cell epitope comprises a carrier protein.

40. (New) An immunogenic composition as claimed in claim 39, wherein the carrier protein and IL-13 element form a fusion protein.

41. (New) An immunogenic composition as claimed in claim 3, wherein at least one short T-cell epitope is added to the IL-13 sequence at a terminal end of the IL-13 sequence by means selected from the group of: synthetic, recombinant and molecular biology.

42. (New) An immunogenic composition as claimed in claim 1, wherein the IL-13 element comprises functional equivalent fragments of the human IL-13 sequence.